(54) Title: SCANNING LASER OPHTHALMOSCOPE OPTIMIZED FOR RETINAL MICROPHOTOCOAGULATION

(57) Abstract

A combination of scanning laser ophthalmoscope and photocoagulator expands the range of clinical applications of the conventional scanning laser ophthalmoscope, being able of simultaneous imaging and microperimetry with the delivery of therapeutic laser applications to the retina in a preferred non–contact mode. The device, including a therapeutic laser source, optic–mechanical Maxwellian view coupling, Maxwellian view control, and real–time electronic registration of the therapeutic beam location, permits precise positioning and dosage of the retinal applications. Additional safety mechanisms include concurrent temperature measurement of retinal application and shutter activation based on digital image processing techniques.

Patent Application

for a

SCANNING   LASER   OPHTHALMOSCOPE   OPTIMIZED   FOR   RETINAL
MICROPHOTOCOAGULATION

Background-Cross   Reference   to   Related   Applications

The invention uses the "Modified scanning laser ophthalmoscope for psychophysical
applications" of United States Patent nº 5,568,208, issued October 22, 1996, and is
related to United States Patent Nº 5,543,866, issued August 6, 1996, entitled
"Scanning laser ophthalmoscope for binocular imaging and functional testing".

Background-Field   of   Invention

This invention relates generally to instruments for examining the eye and specifically
to an electro-optical ophthalmoscope for analyzing retinal function and assisting
retinal microphotocoagulation.

Background-Description   of   Prior   Art

The ophthalmoscope is well known as an important aid for studying and examining the
eye, and in particular, the fundus or retina of the eye. As a result of great interest
in preserving man's eyesight, ophthalmoscopes of various constructions have been built
and used. The latest version of the ophthalmoscope, a scanning laser ophthalmoscope
(SLO), is particularly appealing because of its unique capability of combining the
visualization of the retina or eye fundus with certain psychophysical testing
procedures such as the study of preferred retinal loci of fixation (PRLs), potential
acuity measurements, and microperimetry. With the scanning laser ophthalmoscope, a

unique, precise correlation between retinal anatomy and function can be established. Different stimuli, used in visual psychophysics, can be projected onto the fundus with the help of the scanning laser ophthalmoscope. Overlay graphics are then used to display some stimulus characteristics such as size, location, and intensity on the fundus image in real-time. Detailed functional mapping of the fundus is thereby possible. Such retinal function mapping is now known to be very helpful to the retinal surgeon when planning therapeutic laser to the retina. These laser applications have been until now delivered to the retina with a different instrument. This implies that simultaneous psychophysical testing or even the injection of diagnostic angiographic dyes such as fluorescein or indocyanin green during the laser treatment is impossible. U.S. patent Nº 4,213,678, issued September 29, 1980, discloses a scanning laser ophthalmoscope for the purpose of simultaneously diagnosing and treating retinal disease using two different intensity levels of the scanning laser beam. One intensity range can be used for monochromatic imaging, angiographies or psychophysical testing while a much higher level of the same laser beam or a different colinear scanning laser beam is useful for thermal retinal coagulation. This novel approach however is not ideal because of the technical difficulties in implementing safety controls for such scanning therapeutic laser beam, the difficulty in modulating the scanning laser beam over a range from non-coagulating to coagulating powers at video rate, and the non-thermal complications of a very high intensity pulsed laser beam at video rate. It is nevertheless possible and evident for s/he skilled in the art, to combine optically the scanning laser ophthalmoscope with a traditional non-scanning continuous laser source for the purpose of retinal photocoagulation. This combination, as described on multiple occassions in the prior art, is exemplified by the combination of a traditional slitlamp or indirect binocular ophthalmoscope with a therapeutic laser source. These combinations are typically provided with an aiming laser beam that is colinear with the therapeutic laser beam, a focussing device, a micro-manipulator for positioning the therapeutic laser beam onto the desired retinal location, and a combination of safety shutters and filters that interrupts the photocoagulating laser in case of malfunctioning of the instrument. Also, as proposed before, an analysis of the reflection and backscatter of an appropriate aiming beam immediately before the application of the therapeutic laser to the retina, can reveal localized differences in retinal absorbance for a particular wavelength. This in turn can be useful for the adjustment of the laser power in order to obtain consistent burns of equal intensity on the retina in different locations (Pomerantzeff et Al.). It has also been proposed to use advanced image recognition and tracking to automatically place the laser applications on the retina where desired by the surgeon.

However, until the present invention, all coagulating ophthalmoscopes, including the scanning laser ophthalmoscope, have been limited when consistent minimal intensity laser applications on the retina are desired. The thermal changes caused by such laser applications are very difficult if not impossible to visualize and therefore the desired endpoint of the application is often exceeded. This is even accentuated by the fact that the surgeon, upon recognizing the minimal changes on the retina, will need a minimal reaction time delay to stop the therapeutic laser, and during this interval the laser continues to deliver heat to the retina. Also, it is difficult to avoid re-application of laser to the same area or too close to another laser application because of the low visibility of the effects of a minimal application during the current treatment session or at a later session.

Furthermore, eye movements and changes in the subject's fixation have hitherto limited the accuracy and ease of performing either high resolution microperimetry or applying microscopic laser to the fundus. In the case of microperimetry, a manual "repeat trial on error" presentation of a stimulus to one specific retinal location is possible, using fiducial landmarks as a guide. The procedure however until now corrects the position after the stimulus has been presented. This approach cannot be used when so called adaptive psychophysical testing strategies are involved. They require correction of the subject's changes in fixation immediately before presentation of the stimulus. "Repeat-trial-on-error" is obviously not possible in the case of laser applications. Since the reaction time of the surgeon may exceed 200 ms, a 100 ms application can then be wrongly targeted on the retina in the case of fixation loss. In the case of non corneal contact coagulation, the iris may be inadvertently hit for the same reason. The minimal reaction time of the surgeon also explains why it is a. dangerous concept to have the instrument combine with digital image processing and automated tracking to decide where to treat: in case of malfunctioning or inaccuracy the wrong applications will be placed before the surgeon can even intervene. Automation would also require a precise mapping of the positioning of the micro-manipulator to the fundus coordinates. This coupling is very difficult to realize mechanically, difficult to calibrate and prone to error. At present there is no constant mapping or linkage between the position of the micromanipulator and the position of the aiming beam or therapeutic beam on the retina in any known combination of ophthalmoscope and photocoagulator.

As mentioned in the related U.S. patent, the optical entrance pupil of the Maxwellian view is even more difficult to control manually since usually no reliable fiducial landmarks in the pupillary area are available to the examiner, both in the case of microperimetry or the therapeutic application of laser. In the case of a preferred non-contact photocoagulation technique, i.e. without using a corneal contactlens, it

is desirable to keep the therapeutic beam within the anatomical pupil to avoid hitting the iris.

In microperimetry with the SLO, variations in the entry pupil of the Maxwellian view will introduce a potential Stiles-Crawford effect and variations in threshold measurements due to unequal media absorption or scatter in different optical paths through the ocular media.

Lastly, in order to use microperimetry under desirable minimal background conditions, a large dynamic range of stimulus intensity to surrounding background is required. Simple one-dimensional modulation, whether acousto-optical or through electrical amplitude modulation of diodes, limits this dynamic range.

Objects and Advantages

The principal object of this invention is therefore to provide a single instrument, a scanning laser ophthalmoscope, with the capability of concurrent optimized microperimetric testing, angiographic testing, and preferably non-contact microphotocoagulation with the necessary controls for the dosage and optimal placement of microscopic laser applications.

Dosage can be monitored in real-time through continuous measurement of the heat build-up at the photocoagulation location with an appropriate near infra-red linear detector within the scanning laser ophthalmoscope. The laser application process can then be modified according to the retinal temperature that is measured. Digital image processing techniques are used to obtain optimal placement of the laser applications. In general, this is accomplished by registering the localization of the aiming beam or therapeutic beam in the video raster. Feature detecting algorithms are used for this purpose on either the thermal or optically filtered visible light video images in real-time during the laser application. The therapeutic laser beam can be interrupted if e.g. the current localization of the application no longer matches with a preselected localization on the monochromatic real-time video image of the retina, as determined by digital image processing techniques such as normalized gray scale correlation. With other words, it is now possible with the instrument to deliver very mild consistent retinal laser applications, mostly involving the photoreceptor - RPE complex at predetermined locations and to store these positions as overlay graphics on a reference image of the fundus. This precise mapping can then be re-used for outlining further applications without the risk of retreating unrecognizable previous locations or putting the applications to close to each other. The mapping can also be used in the long term microperimetric evaluation of the impact of laser applications. Several other diverse advantages of the device can be envisioned. In the art of retinal microphotocoagulation it becomes possible to diagnose and treat with the same

instrument in an unprecedented manner. It is possible to perform laser applications and then immediately assess the results with monochromatic or angiographic viewing of the retina, adjusting the treatment if necessary. Microperimetry can instantly verify whether photoreceptors have been destroyed by the laser application; this location can also be marked automatically on a master image for future reference.

In general, the infra-red visualization of the fundus and the possibility of projecting a visible fixation cross within the laser raster enhances the patient's cooperation. Also, the therapeutic laser delivery system can be made non-contact, especially with the help of concurrent imaging of the anatomical pupil. This concurrent imaging allows centering of the therapeutic laser beam and prevents accidental iris involvement in the laser applications. In the 20 degree field of view of the instrument large magnification is achieved on a video monitor, resulting in a high accuracy and relative ease of placement of small laser applications.

Most importantly, the thermal control and automated recognition of the laser application loci permit the creation of non-visible closely spaced minimal intensity applications particularly aimed at destroying the photoreceptor cells while leaving the underlying nourishing choriocapillary and choroid layers fairly intact. The retinal pigment epithelium will then have a better chance to recuperate as well. It is possible to preselect a pattern of laser application loci on the retina. However, the retinal surgeon remains in control of where and when the applications are made since it is s/he who will control the micromanipulator and activation switch. Software such as normalized gray scale correlation will only interrupt or disable the therapeutic laser beam, faster than the surgeon's reaction time, in case of misalignment or overdosage. Unlike proposed automated photocoagulation these are complimentary safety features that will not cause harmful effects if wrongly activated.

U.S. patent 5,543,866 discusses the importance of a binocular evaluation of retinal function. Being able to fixate with corresponding preferred retinal loci in both eyes is a major advantage in low vision rehabilitation. At the other end of the spectrum, pseudocentral fixation, is the most significant impediment to visual re-habilitation. These and other important observations play a role in measuring potential visual acuities and planning laser applications to the retina of patients with age related maculopathy. It has further been demonstrated in microperimetry that absolute retinal thresholds correlate with the amount of photopigment that is present in the retina. Stiles-Crawford functions can reveal the general orientation and degree of alignment of the photoreceptors. Abnormalities in above mentioned parameters measure damage to the retinal pigment epithelium-photoreceptor complex in the retina and this information is useful in the planning and follow-up of laser applications as outlined in Application Ser. Nº 08/207,385. Well-known adaptive strategies have been optimized

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for use with the scanning laser ophthalmoscope to measure the above mentioned
parameters of vision. These strategies measure precisely visual acuity or retinal
sensitivity on the retina and specifically benefit from a combined two-dimensional
acousto-optical and laser diode modulation to increase the dynamic range of stimulus
to background intensity, correction of AOM delay, the use of non-destructive graphics
overlays, combined infra-red and visible wavelength illumination of the retina,
correction algorithms for fixation shifts before stimulus presentation, and
recognition of the entry pupil of the Maxwellian view with an automated, motorized x-
y-z feedback control of the location of this entry pupil. The combination of such
enhancements has never been realized or proposed prior to the invention and is an
explicit object of the invention.

Further objects and advantages of the invention will become apparent from a
consideration of the drawings and ensuing description.

Description of the Drawings

FIG 1 is a diagrammatic representation, illustrating the components of the scanning
laser ophthalmoscope, optimized for microphotocoagulation. Five subparts can be
distinguished. (1) A scanning laser ophthalmoscope proper, with multiple lasers,
detectors, and AOM. (2) A motor block component capable of moving the SLO in the xyz
directions. (3) A therapeutic laser with optical linkage to the scanning laser
ophthalmoscope. (4) The Maxwellian view control components, part of aforementioned
U.S. patent. (5) Human interface elements consisting of monitors, the eye with retina,
and a pushbutton.

FIG 2 illustrates the relation between the different electronical components of the
scanning laser ophthalmoscope-microphotocoagulator. The overlay frame grabber card has
an input interface, frame memory, display interface and CPU interface. Besides the OFG
card(s), the host bus acccomodates a I/O card for interpreting the pushbutton, and
interaction with the control circuit of the therapeutic laser. Also an interface card
for controlling the motors is present. The SLO electronics interface shows the synch
generator, detectors, AOM circuitry and direct electrical modulation of diode laser.
The following circuits are represented: (1) video-in pathway. (2) Video-out pathway.
(3) the synchronization pathway and genlocking of other components of the system
including adc, dac, detectors. (4) The TTL circuit to and from the therapeutic laser
controlling the shutter and communicating activation of the therapeutic beam. (5) The
circuit serving the different motors.

FIG 3 details the opto-mechanical link between therapeutic laser and scanning laser ophthalmoscope.

FIG 4 illustrates the optical ray tracing of either diagnostic or therapeutic beam. Parallel rays in general illuminate the same retinal location but from a different angle. Non-parallel rays will sweep across the fundus. The Gaussian beam measures about 0.5 mm at the pupillary plane and tapers to about 12 micron on the retina plane. Ray tracing has been simplified.

FIG 5 illustrates the effect of a translational shift in fixation. Fixation cross position remains unchanged. Point P on the retina shifts to P'. This is in accordance with the movemement of the small search window within the larger reference window. The search window contains a gray scale feature that can be used in normalized gray-scale correlation.

FIG 6 illustrates the adaptive testing algorithm combining an UDTR transformed response staircase with a four alternative forced choice procedure.

FIG 7 illustrates the correspondance between the bitlevels of the frame grabber board and the power output at the exit aperture of a 129 pixel square. 26 levels have been measured to plot the polynomial regression curve from which all other bitlevels can be derived.

Fig 8 illustrates the adaptive testing algorithm, commonly called PEST procedure, to derive at a final bitlevel, regardless of the stimulus spacing.

Reference Numerals in Drawings

10 Prefocussed Gaussian beam of laser light

12 Posterior pole of the eye

14 Scanners, including polygon and galvanometer

16 Maxwellian view of the illuminating path

18 Reflected and backscattered light from the eye

20 Beam separator

22 Pinhole at the retinal conjugate plane

24 Avalanche photodiode

26 Video display monitor

28 Diode infra-red 780 nm laser

30 Amplitude modulation of diode laser

32 He-Ne red 632 nm laser

34 Pair of adjustable linear polarizers

36 Graphics on the retina, visible as overlays

38 Acousto-optic modulator

40 Electronic circuitry of scanning laser ophthalmoscope

42 Distribution of common synchronization to different components

44 Encasement

46 Beamsplitter

48 Superluminescent 880 nm LED

50 Nose, cheeks and eyebrows

52 Cover of scanning laser ophthalmoscope

54 Slanted window of scanning laser ophthalmoscope with diaphragm

56 CCD videocamera with objective

58 Bite bar

60 Chinrest

62 Vertical movement mechanism using stepper motor

64 Horizontal two dimensional movement mechanism using stepper motors

66 486/33 mHz CPU with overlay frame grabber board

68 Additional overlay frame grabber board

70 Entrance pupil laser beam as overlay on image of anatomical pupil

72 Partial infrared barrier filter

74 Additional graded neutral density filter and diaphragm

80 Therapeutic laser beam

82 Transmission optics

84 Therapeutic coagulator

86 Aiming beam

88 Collimator-telescope

90 Variable aperture

92 Safety filter(s)

94 Electronic interface therapeutic laser

96 I/O link

98 Pushbutton for psychophysical purpose

100 Adjustable mirror hinges

102 Positioning device

104 Framework

106 Support arc

108 Projecting mirror

110 Pivot point of therapeutic laser beam

112 Micromanipulator

114 Second avalanche photodetector with filters

116 Alternative third extended IR sensitive avalanche photodetector

Description and operation of an embodiment

A typical embodiment of the scanning laser ophthalmoscope optimized for micro-
photocoagulation is illustrated in Fig 1 through Fig 3, Fig 4 through Fig 8
illustrate a method of operation of the instrument. The principles of scanning laser
ophthalmoscopy are described in detail in the prior art. Features of the scanning
laser ophthalmoscope relevant to the invention are further discussed.

I. THE SCANNING LASER OPHTHALMOSCOPE

A prefocussed Gaussian beam of laser light, 0.5 mm in diameter 10, is further
focussed by the eye optics to aboutabout 12 μ in diameter at the retinal plane, and is
scanned over the posterior pole of the eye 12 in a sawtooth manner with the help of
scanning mirrors, currently a polygon and galvanometer 14. Both fast horizontal 15
KHz and slower vertical 60 Hz deflections of the flying laser spot are at standard
video RS-170 rates and create the rectangular laser beam raster that is seen by the
subject. A Maxwellian view 16 is used in the illuminating portion of the scanning
laser ophthalmoscope: the pivot point of the scanning laser beam varies minimally
during scanning and is optimally situated in the iris plane with an average waist of
less than 1 mm. Typically a rectangular area of 0.5 cm^2 on the retina is illuminated.
This corresponds to a field of view of 40 degrees in diagonal or 32.7 degrees
horizontally by 23.4 degrees vertically. The field of view can be changed from 40 to
20 degrees by switching optical components. In the 20 degree field of view, the pivot
point of the Maxwellian view is less variable in position during scanning, but wider
in diameter at the entrance point of the Maxwellian view. In confocal viewing the
focussing i.e. positioning of the depth of the waist of the Gaussian beamthen becomes
very critical to the point that it is possible to measure refraction for
psychophysical purposes. Astigmatic errors unfortunately cannot yet be compensated
with the optics of the instrument itself. This would be easy to accomplisch by
incorporating a rotation dial of cross-cylinders. Also in the 20 degree field of view,
it is more difficult to work around focal scattering or absorbing elements in the
ocular media. Separate calibrations are necessary for the 20 or 40 degree field of
view in psychophysical applications.
It is important to understand that the observer will not see a flying spot but rather
a rectangle filled with thin horizontal stripes because of the temporal summation
characteristics of the visual system. The reflected and backscattered light from the
eye 18, now filling the pupil, is descanned over the same mirrors, separated 20 from
the illuminating beam and passed through a pinhole 22 at the retinal conjugate plane

before reaching a fast and sensitive avalanche photodiode **24**. This confocal detection is essential for obtaining high contrast pictures of the retina with infra-red illumination. It is accomplished by eliminating stray light at the pinhole. Non-confocal viewing modalities, also called dark-field, indirect or Tyndall imaging, are obtained by the insertion of a central stop instead of the pinhole **22** or off-axis illumination of the retina. The amount of light on the photodetector is translated into a voltage that modulates the intensity of an electron beam on the visual display cathode ray tube monitor **26**. The electron beam moves synchronically with the scanning laser beam and a real-time video image of the fundus is likewise created on the display monitor. Two laser sources are aligned to illuminate the retina. The two lasers serve a different purpose. A high intensity diode infra-red 780 nm laser **28**, electrically modulated **30** and vertically polarized, is nearly invisible to the subject. It produces the retinal image on the display monitor. A colinear low intensity He-Ne red 632.8 nm red laser **32**, modulated with a pair of adjustable linear polarizers **34** and horizontally polarized, is visible to the eye. It is used to draw psychophysical stimuli **36** in the laser raster for projection onto the retina. These stimuli are created by amplitude modulation of the laserbeam at video rates as the red light passes through an acousto-optic modulator **38**. The acousto-optic modulator is driven by a standard video source, usually a computer overlay frame grabber card that contains the graphics information. This graphics generator is genlocked to the crystal clock of the electronic circuitry **40**. Master timing signals are derived from the spinning polygon. It is important to understand the reason for using at least two different lasers. The scanning laser ophthalmoscope is very light efficient: about three orders of magnitude less light is necessary to visualize the fundus when compared with conventional ophthalmoscopes. However this light is still orders of magnitude the amount used for typical psychophysical testing. The problem is solved by using a 780 nm laser with sufficiently high output and for which the silicon detector of the scanning laser ophthalmoscope, but not the eye, is most sensitive, in combination with a low intensity 632 nm laser, for which the human eye is sensitive but insufficient for visualizing the fundus. This explains also why the stimuli which are perceived by the subject are usually not visible in the retinal picture, unless very bright. The exact position and characteristics of the stimuli can however be shown in real-time on the retinal image with the help of computer overlays as all image video out of the scanning laser ophthalmoscope, scanners, and graphics video into the acousto-optic modulator are synchronized to the same crystal clock **42**.

II. LASERS, MODULATION, AND DETECTION IN THE SCANNING LASER OPHTHALMOSCOPE

In fluorescein angiography with the scanning laser ophthalmoscope, a 632 nm He-Ne laser is usually combined with a 488 nm laser that replaces the functions of the 780 nm laser described above. The 488 nm argon laser is used for excitation of the fluorescein molecules. A 500 nm barrier filter with no pinhole at the retinal conjugate plane is used to separate the backscattered excitation light from the fluorescent light. In indocyanin green angiography with the scanning laser ophthalmoscope, a 780 nm diode laser is kept for excitation of the indocyanin green molecules. A 800 nm barrier filter with no pinhole at the retinal conjugate plane is then used to separate the backscattered light from the fluorescent light. With a prism, 514 nm can be isolated from the argon laser. Many wavelengths can now be produced with a diode laser. Additional beam conditioning is necessary with these lasers.

For example, the diode 780 nm laser 28 can be replaced by a diode laser of longer wavelength, 904 nm. For every 10 nm increase in wavelength of the diode laser beyond 670 nm, the efficiency for stimulating the retina will be reduced to one half. This is useful in making the infra-red background illumination for visualizing the retina on the display monitor even less visible to the subject and this is required for measuring absolute thresholds on the retina. Also longer wavelengths will produce different monochromatic images that may yield useful clinical information. The use of two infra-red lasers in combination with a visible wavelength is an option for binocular scanning laser ophthalmoscopy. In this embodiment each infra-red wavelength will be delivered to one eye and the returned light will be directed to a separate detector. The use of multiple detectors and multiple laser sources has been described in the prior art. Appropriate barrier filters are installed accordingly.

Surface-emitting quantum-well laser diodes combined with a confocal two-dimensional array detector system, are of increasing interest. This approach will offer the advantages of high packing densities on a wafer scale. An array of up to a million tiny individually modulated cylindrical $In_{0.2}Ga_{0.8}As$ surface-emitting quantum-well laser diodes with lasing wavelengths in the vicinity of 970 nm and shorter can substitute the traditional laser sources and scanners of a scanning laser ophthalmoscope. This will render the device more compact, less noisy, and less susceptible to mechanical wear and tear.

The 632.8 nm He-Ne laser 32 has been incorporated in the scanning laser ophthalmoscope because of its compact and sturdy design. It is however also the wavelength of choice for generating graphics and stimuli. Reasons for this preference are the maximal transmittance and minimal scatter within the transparent media of the eye, a minimal interference with the xanthophyll and hemoglobin pigments, and a typical monophasic cone response when compared with shorter visible wavelengths. These

advantages persist if a longer visible wavelength were chosen, e.g. a diode laser at 650 nm.

In traditional Goldmann and automated perimeters, stimuli and background illumination are provided by different optical pathways, the lightsource however being the same. the advantages of this configuration are twofold. First, the background and stimulus fluctuate in the same amount as the lightsource is varying in intensity. Second, additional separate modulation of background and stimulus is possible with a neutral density filter and thereby a minimal or zero background with a maximum stimulus as permitted by the light source, is possible. Unlike the Goldmann and automated perimeters, stimuli and background illumination are always provided by the same optical path and light source in the scanning laser ophthalmoscope and cannot be further modulated with e.g. a separate neutral density filter for each channel. A truly zero background is not possible with either electrical amplitude modulation or acousto-optic modulation and the ratio between stimulus and background has a maximum limit. For acousto-optic modulation, the theoretical limit is 700, 300 is the practical and desired limit but very often only 100 is obtained. Incorporating the 650 nm diode laser can expand the dynamic range of stimulus to background illumination intensity by combining in parallel the electrical high-frequency amplitude modulation of the diode with the acousto-optic modulation described before. For this purpose the blue and red output of the overlay frame grabber board are used. The circuitry is easily constructed by s/he who is skilled in the art of electronics. This set-up requires the electrical amplitude modulation bandwith of the diode to exceed the video bandwith of the SLO. An easier alternative at present is to combine in parallel fashion two acousto-optic modulators, each of which are controlled by the red and blue video out of the frame grabber board. The rise time of acousto-optic modulators can be as fast as 1 ns, bandwith exceeding 40 Mhz.

The measurement of dark-adapted thresholds, dark-adaptation and Stiles-Crawford functions require a minimal background and sufficiently intense maximum stimulus. A dynamic range of maximum stimulus intensity to background intensity of 2.5 log units is acceptable.

As mentioned before, the acousto-optic modulator is driven by a standard video source, a computer overlay frame grabber card that contains the graphics information, and is genlocked to the crystal clock of the electronic circuitry. A typical example of such a video card is the FG 100-AT or more recently introduced, the OFG card, both available from Imaging Technology Inc., Bedford MA. The OFG card is also the essential hardware for alignment and tracking of the pupil or fundus landmarks as described below. Two OFG cards, which are I/O mapped can reside in one CPU, typically equipped with a Intel Pentium microprocessor. The OFG board has to provide three basic functions for realizing the different psychophysical testing and imaging procedures

with the scanning laser ophthalmoscope: generation of 8 bits graphics, frame grabbing
and display of overlays. The different testing algorithms are constructed from an
appropriate sequence of software routines. The method of microperimetry will be
detailed below. The library of basic software routines is, as usual, provided by the
board manufacturer. Specific bitlevels of the graphics board, out of 256
possibilities, are combined with appropriate neutral density filter settings placed in
various positions for approximate and fine tuning of laser light intensities.
Individual bitlevels are translated into corresponding intensity levels by converting
each bitlevel to an analog voltage with the D/A of the graphics board. This output
voltage is then amplified and off-set by the AOM driver electronic circuit to obtain
suitable voltages for modulating the amplitude of a radio-frequency carrier signal.
The piezo-electric transducer of the acousto-optic-modulator is driven by this signal.
Acoustic standing waves are created by the piezo-electric transducer. The atoms of the
crystal then behave as a diffraction grating for the transversing laser beam. The
amount of light passing through the diffraction grating as a first-order beam at the
Bragg angle, defined by the frequency of the radio signal, is directly proportional to
the amplitude of the radio-frequency signal. The time required for the AOM to adjust
the intensity after changing bitlevels is called the AOM delay. The delay has to be
accounted for in calibrating the overlay graphics. Inherent fluctuations in the
electronics of D/A converter, AOM driver, and laser output will not affect the ratio
of light intensities corresponding to any two bitlevels. Short term and long term
variations of individual bitlevel intensities exist. Short term fluctuations are
irrelevant for psychophysics since they are usually smaller than the psychophysical
uncertainty and long term variations are neutralized with the help of a radiometer.
Minimal spatial variations of light intensity also exist within the laser beam raster.
They are neutralized with either software or a graded neutral density filter. Also a
variability in local laser raster geometry has to be taken into account. A pincushion
or trapezoid deformity of the near rectangular raster is caused by the internal
optical configuration of the scanning laser ophthalmoscope. External angular
dimensions of graphics are determined with the arctan formula. On the retina,
equivalent linear distances are calculated using the standard observer's eye of
LeGrand with an effective optical radius of 16.7 mm. 300 μ on the retina equals 60
external minutes of arc. In practice, an uncertainty of about 10 % in absolute size is
expected because of the metric nonlinearities described and the variability in
individual eye optics.

In summary, The laser raster itself is a very unusual for presenting graphics to the
retina, graphics are presented in multiples of 33 ms, the time interval to draw one
complete video frame on the retina. Each video frame consists of two interlaced video
fields of 16.7 ms and 256 lines, the video fields may overlap during eye movements.

Within each video field the graphics is composed of discrete pixels and every pixel is illuminated with a Gaussian beam profile in Maxwellian view for only 77 nanoseconds each. This is in sharp constrast with the smooth delivery of photons to the retina in conventional Ganzfeld, Newtonian illumination of standard perimeters. However the same number of photons arrive on the retina in both illumination systems, but with a completely different spatial and temporal distribution. Under physiologic testing conditions, it has been demonstrated that visual psychophysics is equivalent in both illumination systems.

III. MAXWELLIAN VIEW CONTROL

The configuration of Fig 1, 2, and 3 is for use with the Rodenstock Scanning Laser Ophthalmoscope 101 or 102 (Munich, Germany). This configuration is readily adapted for other embodiments of the scanning laser ophthalmoscope by s/he who is skilled in the art.

The principal optical components for controlling the Maxwellian view of the scanning laser ophthalmoscope-microphotocoagulator are contained in a moulded and closed encasement for the purpose of protection against dust and stray light 44. These components include the beamsplitter 46, optical filters, and illumination source for the anterior segment 48. The encasement is painted matt black on the inside to minimize unwanted scatter, the coating specifically absorbs any reflected therapeutic laser light as described below. The encasement is tapered and provides as much sparing as possible for the bodily parts such as the nose, cheeks, and eyebrows of the subject 50 and has three optical apertures. The outside finishing matches that of the scanning laser ophthalmoscope 52 to which it is fitted tightly as a clip-on, easy to remove if necessary. All three apertures are optionally protected by anti-reflection coated glass, centered on the optical axis, and may contain an optical filter as specified below. The aperture that is closest to the scanning laser ophthalmoscope measures about 5 by 5 cm, and is parallel with the slanted window of the scanning laser ophthalmoscope at 15.6 degrees 54. This is helpful to eliminate unwanted reflections. The front aperture, about 1.5 by 1.5 cm, is facing the subject's eye, vertically, at a comfortable distance as to avoid touching the eyelashes. The third aperture, 2 by 2 cm, is superior or inferior, slanted, and faces a CCD monochrome videocamera with objective 56, which is firmly attached to the scanning laser ophthalmoscope. An appropriate objective would be the 25 mm 1.4 C mount Cosmicar lens from Asahi Precision Co., LTD., Japan with the 5 mm extension tube. An appropriate CCD videocamera would be the Sony XC-75 equipped with a 1/2 inch size interline-transfer CCD. The IR blocking filter has been removed from this camera and replaced by a dummy glass. The CCD camera can be easily removed and is in a fixed position relative to the

encasement, even if the scanning laser ophthalmoscope moves. The axis of the CCD camera is vertical and coincides with the optical axis. The scanning laser ophthalmoscope with the attachments described can move vertically with the help of a software controlled stepper motor **62**. Two other stepper motors realize the horizontal movements of the scanning laser ophthalmoscope on a platform **64**. A computer, equipped with one or two OFG cards, mouse, and keyboard control is provided **66, 68**. An appropriate interface card controls the three motors of the scanning laser ophthalmoscope. One TV monitor displays the eye fundus with graphics overlay using the scanning laser ophthalmoscope **36**. Another TV monitor channel displays the anterior segment of the eye, focussed on the iris with the CCD camera **70**. It can provide the exact position of the optical entrance pupil of the scanning laser ophthalmoscope as an overlay. The monitors, luminous control buttons, and reading light for the examiner are optically isolated from the subject. The only light reaching the subject is coming from the reduced-in-size anterior window of the scanning laser ophthalmoscope. This reduction is size is provided by a simple black diaphragm. It reduces unwanted light from within the scanning laser ophthalmoscope, unmodulated parts of the laser raster, and the horizontal edges of the video-fields that are produced by the horizontal scanning. These edges often have a higher irradiance because of the inertia in the scanning galvanometer mirror.

With a modification and extension of the scanning laser ophthalmoscope optics it is possible to [1] visualize the posterior pole, retina or fundus of one eye in detail; [2] to project graphics, for example a 8 by 8 pixel square that is brighter than the background in Maxwellian view onto the retina; [3] simultaneously view the anterior segment of the eye on the same or different monitor, focussed on the iris plane and unambiguously demonstrating with the help of overlays the exact position of the laser beam in Maxwellian view used to draw the background and stimulus onto the retina; [4] to observe the Maxwellian view entrance pupil of the therapeutic laser beam as desribed in another chapter; [5] all observations do not interfere with each other, the quality of the retinal image does not imply a lower quality of the iris image and the observation of the iris does not interfere with the purpose of psychophysical testing, for example by introducing a bright background; and [6] it is possible to, independently of each other, move the psychophysical stimulus location or therapeutic laser application location on the retina to any desired position and simultaneously, at will, move the scanning laser ophthalmoscope and entrance pupil of the laser beams within the anatomical pupil of the iris. Thereby the point of entry in the pupillary plane can be a variable in psychophysical testing or therapeutic application of laser, where the retinal location is kept unchanged and also it is possible to fix the

entrance pupil while moving the stimulus position or therapeutic location on the retina.

In general, this is realized by [1] introducing a beamsplitter to provide two optical paths, one for the scanning laser ophthalmoscope proper and the second for visualizing the anterior segment of the eye; [2] The introduction of a separate illumination source for the anterior segment with appropriate filters to block unwanted light from reaching the CCD camera. [3] Active or passive stabilization of the stimulus on the retinal image, and selection of entrance pupil of the Maxwellian view system. [4] The use of overlays with an appropriate graphics and videocard for demonstrating the exact position of the stimulus or therapeutic laser location on the retina, and the exact position of the laserbeams in the anatomical pupil. [5] The ability to move, manually or with the help of stepper motors the scanning laser ophthalmoscope relative to the subject, and the stimulus position or therapeutic location on the retina with the help of a pointing device and computer program.

Movement of the scanning laser ophthalmoscope in a frontal plane will cause the rays of the incident laser beams to use a different part of the entrance pupil. This does not cause a significant shift in the position of the focus on the retinal image because the movement will displace the scanning laser beam rays in a parallel fashion, and parallel rays are focussed on the same retinal location. This retinal location will however be illuminated in an oblique fashion and therefore a Tyndall phenomenon can be observed on the monitor, equivalent to the classic dark field microscopy. This is somewhat similar to the use of a central stop instead of a pinhole at the retinal conjugate plane in confocal detection. Angulating the entrance laser beams will result in focussing on different retinal locations.

The separate illumination source for the anterior segment can be a superluminescent light emitting diode LED, a close relative of the laser IR diode. The SY-IR53L is a Gallium Aluminium Arsenide super-high output infrared emitting diode in a T-1 3/4 package. It produces noncoherent, nonpolarized IR energy at 880 nm. 880 nm produces negligible interference with the psychophysical testing or application of therapeutic laser. The dispersion angle at half power point is 20 degrees. This is important to insure a fairly homogeneous illumination of the anterior segment from a short distance. The forward voltage is typically 1.3 V, power dissipation is 20 mA. Therefore a rechargeable NiCd battery pack is ideal to provide several hours of uninterrupted service. The radiant power output is at least 3.4 mW/sq.cm, enough to illuminate the entire anterior segment with a single diode. The small package allows a flexible montage of the diode in the encasement. The illumination of the anterior segment and anatomical pupil does not interfere with the fundus imaging. The wide angle distribution of the light, angulation of the diode, and a combination of partial barrier filters 72 for the therapeutic laser wavelength, SLO infra-red lasers and IR

LED light, together with control of the diaphragm in the objective of the CCD, reduce the interference from excessive backscatter from the different lasers. Purkinje images of the IR LED light are however useful in tracking of the entrance beam in the iris plane. As an example, the IR barrier filters remove most of the convergent 780 nm light during the testing procedure. An example is the Kodak Wratten gelatin filter 87C with no transmittance for 632.8 nm, 0.5 % for 780 nm and more than 90% for 880 nm. Another example is the Kodak Wratten gelatin filter 87 with no transmittance for 632.8 nm, 30% transmittance for 780 nm and more than 90% transmittance for 880 nm. A combination of interference filters with removal of most of the 780 nm and therapeutic laser wavelength is neccessary when using the instrument as as microphotocoagulator. These filters can be selectively removed during calibration of the instrument when it becomes necessary to align the pivot area of the Maxwellian beam of 632.8 nm and therapeutic laser beam with an overlay. The calibration is performed by projection of these different laser beams on a piece of paper that is held in front of the scanning laser ophthalmoscope. This calibration is usually very steady since the beamsplitter, CCD camera and scanning laser ophthalmoscope are fixed relative to each other. The CCD camera is optimally sensitive for IR illumination. The crisp image of the anterior segment with the iris, anatomical pupil, and optionally Purkinje images serve as the fiducial landmarks for the manual or automated x-y-z localization of the entrance pupil of the scanning laser ophthalmoscope. It should be stressed that the pivot point of 632.8 nm does not always correspond with the pivot point of 780 nm, and the therapeutic laser source, and lightscatter will make the pivot point area look much larger than it is in reality, especially if higher energies are used. This is in accordance with the fourth power law of light scatter. Also, only a specific part of the visible entrance location is used for illuminating a specific retinal location and will therefore determine the true point of entry of the laserbeams. This may be different from the average position of the beam sweeping across the retina.

In general, the beamsplitter should favor transmission of 632.8 nm, 780 nm, and therapeutic laser light. Any reflected IR or therapeutic laser light, within the encasement, should be effectively absorbed.

The choice of the dielectric coatings for the beamsplitter 46 depends on the wavelengths used, their polarization status, and the angle of incidence of the laserlight. The ideal beamsplitter is nearly non-absorbing and as such the reflectance will be independent of the angle of incidence of the laserlight. The beamsplitter 46 consists of a single plane-parallel glassplate, 5 by 5 cm, with a partially reflecting low absorption dielectric coating on one side. The other side has an antireflection coating optimized for the angle of incidence of 45 degrees. This will prevent ghost images appearing on the video display monitor. A sample coating is HEBBAR™ (Melles-Griot, Irvine, California). Some beamsplitters are highly polarization sensitive. In a

particular scanning laser ophthalmoscope, the infra-red laser has vertical polarization of the E vector, p-plane with regard to the beamsplitter **46**. The He-Ne laser has horizontal polarization of the E vector, s-plane with regard to the beamsplitter **46**. Often ideal transmission-reflection characteristics can not be realized for all wavelengths involved. The most optimal coating permits a maximum of 780 nm to transmit, a maximum of 632.8 nm to transmit, and most of the 880 nm to reflect. The Melles-Griot, Irvine, California #BTF 001 passes about 50% of the s-polarized 632.8 nm He-Ne light, more than 90% of the p-polarized 780 nm diode IR, and reflects about 20% of the 880 nm mixed polarization IR LED.

Two options exist for equalizing within the laser raster the distribution of irradiant power of 632.8 nm light. As explained before, small differences in intensity occur in the scanning laser ophthalmoscope for various reasons. The acousto-optic modulator can adjust intensities according to the location where stimuli are presented or the differences in irradiance can be neutralized with a custom build graded neutral density filter **74**.

The insertion of an optical filter **74** and beamsplitter **46** in the optical pathway reduces the power of the 780 nm laserlight and therapeutic laser light that illuminates the retina and additionally reduces the amount of light collected by the photodetector from the retina. It is reasonable to use a laser source that is more powerful. This source is already available in the scanning laser ophthalmoscope for indocyanin green angiography and is easily adapted for use with the scanning laser ophthalmoscope-microphotocoagulator.

In summary, one useful addition to the scanning laser ophthalmoscope optimized for retinal microphotocoagulation is the addition of a Maxwellian view control mechanism. This facilitates preferred non-contact photocoagulation since the scanning laser ophthalmoscope itself is a large instrument and the entrance beam is not easily seen by the surgeon operating the instrument. A contact method of photocoagulation would be very difficult to realize because of the inertia of the heavy scanning laser ophthtalmoscope. Abrupt movement of the instrument, however small, can very easily damage the fragile structures of the eye if it is physically connected to the instrument with the help of a contact glass. Other advantages will be evident from a description of the optical linkage between scanning laser ophthalmoscope and photocoagulating light source.

IV. PHOTOCOAGULATOR AND LINKAGE TO SCANNING LASER OPHTHALMOSCOPE

The benefit of a Maxwellian view control of the therapeutic beam **80** has been
discussed. This chapter will describe the optical linkage between therapeutic laser
and scanning laser ophthalmoscope, optimized for a non-contact method. Also, the
important mechanism will be described by which the scanning laser ophthalmoscope and
CPU is made aware of the cartesian position of the therapeutic or aiming laser beam on
the retina, i.e. electronic registration of the retinal application location.
The disadvantages of using a scanning therapeutic laser beam that would be switched
from a low energy to high energy status at the appropriate retinal location
(Pommerantzeff, 1980) have been discussed before. Therefore, the therapeutic beam **80**
should be maintained stationary, and allowed to move between laser applications only,
using special transmission optics **82**. The coagulator **84** itself is well known in the
art, either argon or currently diode laser, having the possibilty of emitting
different wavelengths, in particular 514 nm. Often a second colinear low power aiming
beam **86** is provided. Alternatively, the therapeutic beam can serve as an aiming beam
at much lower intensity. Also included in the optical pathway are a collimator-
telescope **88** and variable aperture **90** for precisely adjusting the shape and size of
the Gaussian therapeutic laser beam. An important element of the photocoagulator is
one or more safety shutters **92** or filters. A radiometer is build in to monitor power
output. An electronic interface **94** connects the aforementioned elements with a
control panel that is supervised by the surgeon. In addition, the combination scanning
laser ophthalmoscope-microphotocoagulator has an important I/O link **96**, often a
combination of TTL circuits, between the control circuits of the therapeutic laser and
the host bus of the CPU. This electronic connection can make the CPU aware of when
exactly the therapeutic laser is activated and also provides a means for activating
the safety shutter under CPU control. Such TTL circuit has previously been described
to connect a pushbutton **98** for psychophysical applications to the CPU. The optical
connection between the exit aperture of the laser and a positioning device is
preferably made by a combination of extendable mirror hinges **100**, instead of flexible
fiber optics, in order to tranmit a near perfect Gaussian beam of laser light. Non
fiber optics permit focussing to a smaller waist of the Gaussian beam with a
relatively large diameter entrance optical pupil. Precise positioning in depth and
small retinal applications are possible with this microphotocoagulation technique. A
specially constructed positioning device **102** consist of a framework **104** that permits
a support arc **106** to slide across. On the support arc is mounted a projecting mirror
108. This mirror can also slide along the arc and reflects the therapeutic laser
light from the other mirrors in the transmission optics. The two sliding movements
allow the mirror to project the therapeutic laser beam perpendicular to a curved

surface, e.g. a part of a sphere, such that the therapeutic laser beam will have a
pivot point 110 very similar to the pivot point of the Maxwellian view of the
scanning laser ophthalmoscope. The mirror mount itself is moved with the help of a
micromanipulator 112 that is handled by the surgeon. Typically the positioning device
is about 100 mm by 100 mm and will fit into an existing scanning laser ophthalmoscope
to which it is fixed with support mounts. The Gaussian therapeutic laser beam
typically has an effective 0.5mm to 2mm diameter ($1/e^2$). Power output is in the mW
range, i.e. more than 1000X the output of the diagnostic scanning beams. The beam is
prefocussed by the collimator-telescope lenses of the photocoagulator and further
focussed by the eye optics to a spot as small as 10 μ on the retina. This spot
corresponds to the waist of the Gaussian beam. A highly reflective beamsplitter for
the therapeutic wavelength but very transparant for the other wavelengths of the
scanning laser ophthalmoscope such as 632.8 nm and higher is coated according to the
principles outlined above for the Maxwellian view control. This beamsplitter renders
the therapeutic laser beam and various scanning laser beams of the SLO coaxial towards
the retina. Some therapeutic laser light is however permitted to pass the beamsplitter
in order to reach a photodetector 114 after returning from the retina. The
transmitted light through the beamsplitter and not going towards the retina is
carefully absorbed to avoid confusion with the therapeutic laser light that is
returning from the retina. All detectors are genlocked to a common time base for
producing video output. This is useful in localizing the therapeutic laser spot onto
the retina. For this purpose the detector is provided with a barrier filter to
eliminate all light returning from the retina except the therapeutic laser wavelength.
It is well known in the art of digital signal and image processing to retrieve the
position of the isolated flash of light in the video-signal. Because of the common
time base of infra-red SLO video images and the detector used for localizing the
therapeutic laser beam, a precise indication of the x-y-z position of the therapeutic
beam waist is possible using the confocal imaging of the SLO and overlay graphics.
This information can then be stored, retrieved and further image processed. Several
applications will then depend on the principle or mechanism outlined above. E.g. It is
possible to plan laser applications in particular locations, it is further possible to
store the treated locations for future reference and since the determination of the
coordinates of the therapeutic laser beam is happening in real-time, image
registration as outlined below can determine whether the intended laser application
location is still selected within a radius of acceptance. If misalignment occurs, the
TTL circuit can rapidly interrupt the therapeutic laser beam. This is advantageous
since such interruption is likely to occur faster than human reaction would allow.
Another possibility exists to register the localization of the therapeutic laser
application during treatment. The eye can be considered an imperfect blackbody

radiator at 37 degrees Celsius or 310 degrees Kelvin. The therapeutic laser beam will

warm up the tissue locally, e.g. gradually towards the coagulating temperature of 60

deg C. The peak intensity of such blackbody radiation is situated around 8 - 9 μ

wavelength. It is very much less (< than $10^{6)}$ between 1 and 1.2 μ. A very sensitive

and fast linear infra-red detector 116 can only be used between 1 and 1.2 μ because

the contents of the eye effectively absorb nearly all IR beyond 1.4 μ. Using the

recently introduced linear extended wavelength (1-3μ) photodetectors based on In_xGa_xAs

technology (Hamamatsu, Japan) it is however possible to measure the temperature versus

duration of application at videofield time intervals. Again the detector is gen-locked

to the other components of the scanning laser ophthalmoscope to provide a common time

base. Mirrors and lenses are also optimally coated for the extended IR wavelengths up

to 1.4 μ. and the various beamsplitters should allow the extended IR to pass without

significant loss. Diverse applications of knowing the temperature rise can be

envisaged. It is e.g. possible to produce consistent minimal intensity laser

applications, just intense enough to permanently disable the photoreceptors without

causing further significant damage to the neighboring tissue. The importance of such

approach has been stressed before. Simultaneous psychophysics, an advantage of the

combination scanning laser ophthalmoscope-microphotocoagulator, allows the

verification of the destruction of the photoreceptors. The practically invisible laser

application locations can be permanently marked with overlays as explained above.

In summary, the described preferred embodiment of optical linkage between a scanning

laser ophthalmosocope and photocoagulating light source, including Maxwellian view

control, mechanical Maxwellian view positioning device and common time base

synchronization of various detectors allow the precise placement and registration of

minimal intensity laser applications and associated psychophysics on the retina.

Another advantage of the SLO-microphotocoagulator is the absence of accomodation

induced errors in positioning of the laser spot.

V. PSYCHOPHYSICS OPTIMIZED FOR THE SCANNING LASER OPHTHALMOSCOPE

Several techniques or methods have to be combined to successfully perform

psychophysics with the instrument. These include the generation of computerized

graphics, projection of these graphics onto the retina using a dual laser system

described before, the use of overlay graphics, adjustment of the acousto-optic

modulator delay, correction for shifts in fixation and eye movements in conjunction

with adaptive testing strategies to determine either retinal sensitivity or visual

acuity on the retina. Several key electronic components support these techniques or

methods. They include the overlay frame grabber card, acousto-optic modulator, computer with I/O devices attached.

Indispensable for handling the video that is output by the scanning laser ophthalmoscope and for the generation of graphics that will be projected onto the retina is the overlay frame grabber card, Fig 2. For our applications until now, we used an Imaging Technology OFG card in a 90 Mhz Pentium PC. This card can select between four video input sources, and digitizes the incoming video signal to eight bits of accuracy, at a rate of 60 fields per second (RS-170). On board frame memory can store two 512 by 480 pixel video frames. This versatility is important e.g. for the software algorithms that correct for fixation shifts in microperimetric testing and the multiplexing of the signals from a multidetector SLO. It is also important in simultaneous recording of the entry position of the SLO Maxwellian view and the area that is stimulated on the retina. This relevance will be discussed below. The analog-to-digital converter on the frame grabber has programmable negative and positive reference values for calibrating the white and black video signal levels. A look-up table (LUT) controls the input video and can be used for preprocessing contrast and intensity. This feature is particularly useful in facilitating normalized gray scale correlation as further explained. An additional four bits per pixel controls the very fast switching between different output LUTs for individual pixels. Three independent output channels are provided. The output channels generate RS-170 video for pseudo-color display. Fast switching between output LUTs is an elegant solution for programming non-destructive graphic overlays. Non-destructive graphic overlays drawn into the incoming video signal are crucial for generating the stimuli in the laser raster of the SLO and on the display monitor. Typically, the green output video will deliver the retinal image virtually unchanged to the monitor together with a symbolic graphics overlay outline of the stimulus. The blue output of the original video signal is transformed into a graphics pattern. It is used to control the acousto-optic modulator and defines the background and stimulus that is visible to the observer. The remaining red output can be used for different purposes. One option is a simultaneous control of the electric amplitude modulation of a diode laser. Combined with an acousto-optical device, the dynamic range of modulation can then be dramatically increased. This increase is desirable in measuring more precisely near absolute thresholds in microperimetry. Another critical feature of the frame grabber is the possibility to synchronize to an external video source using the phase-locked loop. This is important since the timing signals provided by the high speed rotating polygon are slightly irregular. Gen-locking (e.g. provided by a time base corrector) is also necessary when analog output from a video casette recorder is used to drive the acousto-optic modulator.

At present, an acousto-optic modulator 38 is used to generate the video graphics in
the laser beam raster of the scanning laser ophthalmoscope. Usually, the digital to
analog video generator of the graphics board produces an analog voltage corresponding
to the bitlevel of the current pixel in the blue channel. This 0 - 1 V output voltage
in turn modulates the amplitude of a 40 - 100 MHz radio frequency carrier signal that
is produced by the AOM driver. The high bandwith, exceeding the video 10 MHz,
guarantees precise modulation of single pixels. The amount of modulation can be
controlled with offset and gain potentiometer controls. These values determine the
shape of the AOM modulation curve and are therefore important in calibration of
microperimetry. The AOM is a special crystal (e.g. fused quartz) in which standing
acoustic waves, causing localized differences in refractive index, are created by a
piezo-electric transducer. The transducer itself is controlled by the modulated radio
frequency signal. The vibrating atoms of the crystal behave as a diffraction grating
for the transversing laser beam. Constructive interference of reflected light within
the crystal generates higher order beams. The amount of reflected light is
approximately linearly proportional to the intensity of the sound waves or modulation.
A maximum transfer of energy from an undiffracted 0th order beam to the 1st order beam
will only occur at a specific angle of incidence: the Bragg angle. Bragg angle,
velocity of sound in the crystal and frequency of the carrier signal are related to
each other. It is important to position the AOM carefully in the optical path to
obtain a maximum range for modulation purposes. The Bragg angle used is very small,
approx. 6 - 15 mrad. It is very difficult to adjust, and one of the principal reasons
for loss of maximum intensity over time. With proper alignment, better than 85 % of
the incoming light can be shifted from the 0th order to the 1st order beam, delivering
up to 150 μW of modulated 632.8 nm light at the exit aperture of the SLO. Changing the
intensities through the acousto-optic modulator takes time. The time is necessary for
the standing sound waves to adjust. This happens at a much slower speed than the
changes that occur in the video display. As a result, a time delay exists between the
update of intensity information in the graphics overlay on the monitor and the actual
change in intensity visible to the subject in the modulated laser raster. Calibration
is of great importance (and has even medicolegal consequences) in assuring the
correspondence between what is seen on the monitor and what is seen by the observer.
The AOM delay can be calibrated by adjusting the position of the real image on the
monitor of a bright stimulus that is projected on the wall to match its overlay
component. This is accomplished by programming the drawing of graphics to the SLO and
to the monitor with an appropriate pixel interval (about 50 pixels or 3.5 μs). Another
very important function of the AOM is to provide the blanking of the video signal

during the retrace intervals. This will prevent the visible scanning laser beam from
being visible during vertical retrace.

We have previously discussed the importance of calibrating the acousto-optic modulator
delay, and the positive and negative video reference values of the graphics board.
These values are stored in a configuration file and can be adjusted if changes have
occurred in the scanning laser ophthalmoscope. Further calibration concerns the size
of the laser raster and light intensities corresponding to the different bit levels of
the video board. One bit level has to be specified as the background intensity. It
usually corresponds to "255" when darker than background stimuli are used or "0" when
brighter than background stimuli are used. An intermediate value of "128" is useful to
generate a finer gradation of stimulus intensities relative to the background. The
drawback is a reduction in dynamic range of the intensity scale.
A set of linear polarizers is used to control the intensity of the 632.8 nm laser
light before it reaches the AOM. 12 predefined filter positions have to be calibrated.
An additional set of external ND filters and selective wavelength barriers can be
added to the instrument. E.g. Melles-Griot filter FG# 3 will transmit 792 nm at over
90 % and reduce 632.8 nm to 6.3 %. Microperimetry software has to be aware of the
background definition, attenuation factors of all ND elements, the normalized AOM
calibration curve and absolute output of the laser at maximum settings in order to be
able to calculate meaningful values of stimulus and background. Stimulus and
background are preferably expressed in trolands, as Weber fractions, or dB values of
attenuation of the maximum possible stimulus. "dB" values can be translated to those
units used in automated static perimeters. "dB" values used without specifying
explicitly the intensities of background and maximum stimulus are meaningless.
The AOM calibration curve of Fig.7 has been obtained using a microprocessor
controlled laser radiometer "lasercomp" from EG&G GammaScientific, Inc, San Diego, Ca.
Calibration is traceable to the National Institute of Standards Technology and in
complete compliance with MIL-STD-45662A. The silicon detector with an area of 100 sq.
mm is connected through a RS-232 serial interface to the same multitasking computer
that projects a graphics square of 192 pixels, centered within the laser raster, onto
the detector. The square itself is shielded from the adjacent areas with the help of a
dark screen. The detector is closely fitted to the optical head of the scanning laser
ophthalmoscope. Stray light is eliminated. The residual dark current from the
photodiode detector is auto-subtracted. For power readings in Watts, the time constant
variable of the current-to-voltage circuitry is adjusted until a maximum and stable
reading is obtained for each bitlevel. This is important because the video timing
introduces fluctuations in the output of the laser source. Other precautions have to
be taken during intensity calibrations. The diode 792 laser within the scanning laser

ophthalmoscope is still emitting power, even at the "0" amplitude modulation settings.
This leakage power is neutralized with the help of an additional external IR barrier
filter, Melles Griot # KG3 that passes 65 % of the light at 632.8 nm and reduces the
792 nm to 4 %. The following conversion formulas have then been applied to convert
Wattage into Troland values: (a) a 192 pixel square is equivalent to 0.112 sq. cm on
the retina; (b) V(1) at 632.8 nm is equal to 0.247; (c) 100,000 Td equals 52.6 μW/sq.
cm on the retina at 555.0 nm. As a result, 1 μW/sq. cm retinal irradiance at 632.8 nm
corresponds to 455.9 Trolands. Conversions to equivalent asb and cd/sq. m are easily
made. (The Troland value could eventually take into account the Stiles-Crawford effect
and losses through the media to arrive at loss-corrected effective Trolands.) Small
variations (in the order of 10%) exist within the laser raster. The output of the He-
Ne laser itself fluctuates over time and during warming-up of the instrument.
Variations of 7 % have been observed. Most variations in intensity output are
physiologically insignificant. The normalized shape of the AOM curve seems invariant
over time as long as gain and offset values remain unchanged. This facilitates
recalibration. Twenty-six bitlevels are routinely measured. These measured values fit
a polynomial of the 5th degree with high degree of correlation. The polynomial can be
reconstructed with as few as 6 samples for recalibration purposes, according to
Lagrange's interpolation method. Curve fitting has been used to obtain the best
fitting polynomial. From this function the corresponding Troland values of the
remaining bitlevels are derived. These calculated values are within 2 % of the
measured values, an acceptable tolerance for perimetric purposes. The main advantage
of a curve fitting method, instead of a fixed conversion table containing all
bitlevels, is the substantial time saved during recalibration. When inspecting the
calibration curve in Fig. 7, it becomes apparent that the gain factor could be
slightly optimized. An increase of the gain will maximize the upper bitlevels in the
sigmoid curve. The offset value could be adjusted in such way that the minimun of the
curve is truly the inflection point at bitlevel 0. As such, the quotient I_{max}/I_{min}
could be improved from a current 36x to about 300x. A value of 300x is typical for a
good acousto-optic modulator and indispensable for measuring near absolute thresholds
with 632.8 nm light.

In size calibration, the same 192 pixel square at maximum intensity, is projected onto
the wall. The square is slightly trapezoid because of the positioning off-axis of the
mirrors in the SLO. In the 40 degree field of view, this square will measure about
13.4 cm on a side while the distance from the pivot point to the wall amounts to 67
cm. Using the Arctan formula, the conversion factor of 3.5 external minarc/pixel or
1.73 minarc/pixel in the 20 degree field of view will be obtained. On the retina,
equivalent linear dimensions are calculated using the standard observer's eye of
LeGrand with an effective optical radius of 16.7 mm, unaccommodated. A Goldmann III

equivalent stimulus would correspond to 20 minarc on a side. The smallest acuity letter E that can be projected has a gap size of 1 pixel and corresponds to 20/34. Ametropia correction, held as close as possible to the eye, will minimize deviations from the standard eye metric and will also reduce the size variations when moving the Maxwellian view along the optical axis. Non-linearities exist towards the edges of the laser raster. It is therefore important to select a reference point for the correction of fixation shifts close to the area where the stimulus is projected. A decimal visual acuity of 1.0 corresponds to 20/20 and per definition is equivalent to 1 external minarc gap size. This corresponds to 4.86 μ on the standard retina. If the 192 pixel square is not equal in length on all sides, then a potentiometer adjustment is necessary to alter the vertical size of the laser raster and equalize the length of all sides.

Two fundamental properties of retinal functioning, acuity and sensitivity, can be efficiently measured with microperimetry. Adaptive paradigms are essential to measure these variables. Quantitative microperimetry relies specifically on the efficiency, accuracy, and standardized approach that is provided by these selected algorithms. In adaptive strategies the decision to present a stimulus of a certain size or intensity is decided by the program on the basis of the subject's performance so far. An adaptive procedure usually defines at what level to start, when to change the level, how much to change and finally when to stop and how to calculate an estimate of the threshold. Particular to the SLO, a decision has to be made whether to correct for fixation shifts before or after presentation of the stimulus.

The preferred algorithm for estimating visual acuity applies a well known up-down transformed-response (UDTR) rule to a four alternative forced-choice strategy. Fig. 6, During the run of the staircase, a letter E is presented with one of four possible orientations. Gap size starts at 6 pixels. Contrast and background can be adjusted but are normally set to maximum and bright photopic respectively. The duration of presentation of the letter E can vary from 0.1 s to continuous. A separate fixation cross, also adjustable in size and contrast is optional. It is used when measuring acuities in other locations than the preferred retinal locus for fixation or PRL. In this situation it is necessary to limit the duration in order to prevent the optokinetic reflex, but long enough to allow recognition. Fixation shifts are corrected in the same manner as discussed in the next paragraph. Most often the acuity at the PRL of fixation is measured. In this case, the E is projected continuously onto the fundus. After presentation, the subject is asked to communicate the orientation to the examiner who in turn communicates the response to the computer using the arrow keys of the keyboard. This buffering guards against wrong input from inexperienced

subjects. The subject is asked to guess when the letter E's orientation is not clear

to him or her, a powerful method to reduce the bias from both the subject and examiner

to a fixed level. With 4 alternatives, the probability of answering correctly by

chance on two consecutive trials is 1/16. A potential acuity rather than real acuity

is measured since it is possible for the examiner to circumvent media opacities and

correct for refraction anomalies. When pseudofixation occurs, a frequent observation,

the subject can be asked repeatedly to eccentrically view the letter E.

The algorithm proceeds quickly in the search phase, starting off with a gap size that

reduces by 1 pixel after two correct answers. This phase familiarizes the subject with

the procedure. The search phase ends after two consecutive mistakes. In the tracking

phase of the computerized algorithm, two correct answers are required before the

algorithm proceeds to a smaller size. One wrong response leads back to the larger

letter E. "0" pixel gap is a valid option. The average pixel gap size of the letter E

is calculated from five staircase reversal values and defined as the acuity threshold.

This approach estimates the 0.71 point of the underlying acuity psychometric function

and aims at correspondence with clinical chart based methods of acuity testing where

one would accept two mistakes out of ten on the chart line acuity. All the trials in

the staircase procedure are stored and graphically displayed, together with an

indication of orientation and whether correctly answered or not. The average pixel gap

size is converted to minarc by multiplying with the appropriate conversion factor. The

reciprocal of the minarc value yields the decimal acuity. According to Ludvigh's data,

minarc acuity drops linearly with retinal eccentricity, hence the usefulness and

advantage of a linear scale in extrafoveal fixation. The limited number of steps

between reversal values is a result of the fairly large step size of 1.73 minarc/pixel

and doubled in the 40 deg field of view. This has to be taken in consideration when

interpreting better than 20/34 acuity values in the perifoveal area or acuities better

than 20/70 in the 40 deg field of view.

The preferred algorithm for estimating retinal sensitivity uses an adaptive yes-no

strategy wherein adjustable steps are determined by immediately preceding trials. The

algorithm is modelled after Taylor & Creelman's "parameter estimation by sequential

testing" or PEST. The procedure is summarized as follows. Fig. 8.

Background is selected. An optional fixation cross of variable size and intensity is

used. Stimulus size and duration are selected. Normal default values are 20 minarc on

a side and 0.1 s. Up to 16 test locations can be selected for multiplexing. Each

location can have a different suprathreshold starting value. The subject's response is

again buffered by the examiner. The stimulus bit value is decremented by the initial

step size of 16 with each presentation until a reversal of the subject's response

occurs. Upon reversal the step-size is halfed. This continues until the minimal step-

size is reached. The final stimulus bitlevel that is calculated is defined as threshold. Some means of recovery from steps in the wrong direction is provided. A third step in the same direction will again double the step-size and continue to double with each further step in the same direction unless a reversal will follow the doubling of a step-size, in which case three step-sizes in the same new direction are necessary before doubling. Doubling occurs until the maximum of 16 bitlevels is reached. The testing procedure is characterized by a variable run length, a high degree of robustness against attention loss and errors from the subject and the important advantage of not requiring decisions about stimulus spacing. Precise stimulus spacing is very difficult to accomplish with the acousto-optic modulator. All bitlevels are now useful for the estimation of the threshold but it is only the final bitlevel that will be converted to a Troland value.

Corrections for eye movements during fixation can be made immediately before stimulus presentation or immediately after stimulus presentation. This depends on the necessities of the testing procedure.

If the stimulus presentation belongs to a predefined grid of test locations or is part of an adaptive strategy, then correction for the displacement vector is necessary just prior to presentation under real-time conditions. For this purpose, any landmark close to the stimulus site can be used. The translational displacement vector is instantly calculated from the difference in cartesian coordinates of the landmark on the initial fundus image that was used to define the grid or location for threshold measurement, with the coordinates on the last image prior to presentation. The landmark coordinates are entered into the computer by the examiner with the help of a pointing device. Hitting the landmark is at times at difficult task. A frozen image at the time of presentation makes it easier to verify to the landmark has been hit. In case of mismatch, the trial can be repeated.

If the stimulus presentation is static but does not belong to a grid or algorithm, a correction for fixation shifts is necessary immediately after the presentation in order to present the individual trials on a single final image in the correct location. This approach is very flexible but much less rigorous than the previous method. Both correction methods also plot actual fixation samples in the correct place on the retinal image.

A continuously presented stimulus is very efficient to explore the central visual field prior to the selection of appropriate static test locations and starting values. Precise plotting of a traditional isopter segment is only possible if a correction is made for the subject's reaction time. This could now be accomplished on-line using the two image buffers of the frame grabber, optionally combined with automated registration of image displacements.[31]

VI. FUNDUS AND PUPIL TRACKING WITH THE SCANNING LASER OPHTHALMOSCOPE

As mentioned before, the entrance pupil and stimulus location on the retina can be selected independently from each other and are subject to a passive or active feedback mechanism to ensure their position regardless of eye movements or fixation shifts. The passive mechanisms include a manual repositioning of the stimulus or entrance beam using fiducial landmarks. A simple repeat trial upon error strategy is used for presenting a stimulus to one specific retinal location under visual feedback control as described in a previous paragraph. Typically the pivot area is focussed on the iris using 632.8 nm light, prior to testing. The distance between iris and scanning laser ophthalmoscope is verified at regular intervals.

The active mechanisms make use of digital image processing techniques for pupil and fundus tracking. A second OFG board 68 within the same CPU can perform these tasks using for example a technique called two-dimensional normalized gray-scale correlation. Such software is provided by Imaging Technology, Inc, Bedford, Ma. A 7 degree rotational tolerance and 60 ms search time are acceptable for the rather liberal requirements in clinical testing procedures. For pupil tracking the reference picture is the anterior segment, for retina tracking it is the fundus image. Feedback regarding eye movements and fixation shifts can then be used to adjust the x-y-z stepper motors 62, 64 or the psychophysical test algorithm as described before Fig 4,5. It is possible to multiplex both video coming from the scanning laser ophthalmoscope and CCD camera. Therefore one computer with two boards is sufficient. In two-dimensional normalized gray-scale correlation a search patttern is retrieved within the larger fixed reference pattern. Multiple search patterns can coexist. A reliable method to lock the antero-posterior distance of the scanning laser ophthalmoscope to the iris is the quantification of the size of different fiducial landmarks within the image of the anterior segment. These can include the Purkinje images.

Summary, Ramifications, and Scope

The scanning laser ophthalmoscope-microphotocoagulator is an electro-optical device that broadens the range of clinical applications of the conventional scanning laser ophthalmoscope. The three cardinal features are a special Maxwellian view coupling device, control over the Maxwellian view entry location, and computer awareness of the location of aiming beam or therapeutic beam through usage of a common time base between different detectors.

With the device it is possible to visualize the retina and simultaneously perform
microperimetry for the purposes documented in the related U.S. patents. Without
changing instruments, the capability now exists to administer laser applications to
the retina. Not having to change instruments, with different optical characteristics,
is an important issue because of the instantaneous feedback with regard to the
angiographic pattern and psychophysical response that one can obtain even during the
treatment session. This feedback is represented on the same image that is used to
direct the laser applications and will therefore enhance the precision of the
treatment. A so called non-contact method of therapeutic laser is possible for two
main reasons. First, a specific optical linkage mechanism between the scanning laser
ophthalmoscope and the terapeutic laser that allows the use of essentially the same
Maxwellian view for both the therapeutic laser and the scanning laser ophthalmoscope.
Second, the use of the Maxwellian view control described in previous U.S. patent, to
verify the presence of the pivot point of the therapeutic laser within the anatomical
pupil of the eye. This positioning could be maintained either passively by the surgeon
or actively using digital image processing on the image of the anterior segment of the
eye. It is e.g. possible to interrupt the therapeutic beam when it inadvertantly hits
the iris margin. The use of mirror-optics and transmission instead of fiber optics
allows a well-defined Gaussian beam to enter the eye. Especially in the 20 degree
field of view, it is possible to manipulate the antero-posterior position of the
minimal waist of such therapeutic laser beam. This focussing permits some additional
adjustment as to the depth of impact of the laser application in the retina. Selective
targetting of the photoreceptor layer is then made somewhat easier with the proper
selection of wavelength, size, intensity, and duration of the laser application. The
ability to concentrate the thermal destruction to the photoreceptor-pigment epithelium
complex may be very useful since selective removal of metabolically very active
photoreceptor elements will reduce the consumption and competition for oxygen, glucose
and other necessary elements, of which the transportation across the diseased retina
is already impaired in early stages of age related maculopathy (e.g. thickening of
Bruch's membrane, soft drusen permeability). The improved oxygenation, provided the
choriocapillary layer is largely kept intact, in turn can reduce the production of
angiogenetic "stress" stimuli produced by the RPE complex and in this way avoid the
neovascularisation stage of age related macular disease. This mechanism may also lead
to the dissapearance of the drusen by reducing the workload of, and enhancing the
productivity of the photoreceptor phagocytosis and renewal cyclus. Microperimetry is
useful to select the areas for laser treatment and then to follow-up on the functional
status of the retina between the non-confluent applications. Possibly retinal areas
with dimished retinal function are more likely to attract new vessels and therefore
should be eliminated first. The laser treatment should respect potential conjugate PRL

of fixation and the horizontal meridian, as much as possible. Microperimetry can be used to verify that a particular area on the retina has been destructed because it should result in a dense scotoma. This is important since minimal applications, e.g. controlled by the thermal detector, are hardly visible. The applications however can be permanently marked on any retinal image using overlays. These overlays of the location of the aiming or therapeutic laser beam are indeed possible because of the use of a gen-locked detector in combination with appropriate barrier filters and image processing. This detector can be the thermal IR or regular visible wavelength detector as previously explained.

Human reaction time is longer than 250 ms. Digital image processing can see faster any misalignment from an intended laser application location or a rapid increase in temperature. Digital image processing can effectively reduce the reaction time to one videoframe.

Microperimetry applications now incorporate all the necesary features for accurateness: fast overlays, AOM delay control, normalized gray-scale correlation for fundus and pupil tracking, and adaptive strategies to determine key parameters of retinal function. Fundus location as well as Maxwellian view entry location can be variables in microperimetry to derive these key parameters.

Although the description above contains many specificities, these should not be construed as limiting the scope of the invention but as merely providing illustrations of some of the presently preferred embodiments of this invention. Other embodiments of the invention including additions, subtractions, deletions, or modifications of the disclosed embodiment will be obvious to those skilled in the art and are within the scope of the following claims. The scope of the invention should be determined by the appended claims and their legal equivalents, rather than by the examples given.

Claims: I claim:

1. A combination of a scanning laser ophthalmoscope and a photocoagulator to enable the placement of laser applications onto a retinal location under simultaneous and continuous observation of said retinal location and its neighborhood, comprising the elements of:

A. said scanning laser ophthalmoscope, having at least two laser sources from which a visible laser beam is used for generating a visible laser raster that contains graphical stimuli and is projected onto the retina, and another essentially invisible and colinear laser beam of sufficient power output is used for obtaining a video image of said retinal location and its neighborhood with photodetecting means of said scanning laser ophthalmoscope on a monitor;

B. said photocoagulator comprising a therapeutic laser source from which a therapeutic laser beam of sufficient power output can produce said laser applications onto said retinal location, further including a colinear aiming beam, a micromanipulator to direct said colinear aiming beam and said therapeutic beam onto said retinal location, pre-focussing means for said therapeutic laser source, and supporting electronics controlling the size, duration and intensity of said laser applications;

C. means for optically coupling said scanning laser ophthalmoscope with said photocoagulator including optical elements selected from the group consisting of mirrors, barrier filters, bandpass filters, interference filters, polarizing filters, apertures, absorbers, beam shaping devices, and liquid crystal filters placed in the optical path of said scanning laser ophthalmoscope and said photocoagulator so that the production of said laser applications does not oversaturate said photodetecting means of said scanning laser ophthalmoscope;

D. a computer with an overlay frame grabber card, said overlay frame grabber card including means for synchronizing video input and video output to timing signals provided by said scanning laser ophthalmoscope, further having sufficient on-board memory and at least three independent output channels so that said computer with overlay frame grabber card is capable of simultaneously digitizing and manipulating in real-time video images of the retina, incorporating said retinal location and its neighborhood, generating said graphical stimuli for projection onto the retina, and indicating the correct location of said graphical stimuli, said aiming beam and said therapeutic laser source onto said monitor;

E. modulating means for said visible laser source to create said graphical stimuli in said visible laser raster using said computer with overlay frame grabber card for indicating the correct location of said graphical stimuli onto said monitor;

whereby it becomes possible to continuously visualize said retinal location and its neighborhood using non-bleaching light levels on a monitor, project a fixation target, position simultaneously said aiming beam onto said retinal location, activate said therapeutic laser source for a variable amount of time while monitoring the position of said retinal location, and from time to time examine angiographically or psychophysically said retinal location and its neighborhood without the need of swithing from said scanning laser ophthalmoscope to a different diagnostic instrument or interrupting the observation of said retinal location and its neighborhood.

2 The combined scanning laser ophthalmoscope-photocoagulator according to claim 1, wherein means for optically coupling said scanning laser ophthalmoscope with said photocoagulator includes:
A. a succession of flat mirror interfaces and structural support means joined together so that enough degrees of freedom exist to move last mirror freely on a virtual surface that is curved in such manner that a pivot point is created for said therapeutic beam, similar to the pivot point of said visible and said invisible beam;
B. said optical elements selected from the group consisting of mirrors, barrier filters, bandpass filters, interference filters, polarizing filters, apertures, absorbers, beam shaping devices, and liquid crystal filters;
C. a beamsplitter; whereby said therapeutic beam and said visible laser beam can be rendered approximately colinear before reaching said retinal location in the eye.

3. The combined scanning laser ophthalmoscope-photocoagulator according to claim 1, further comprising the improvement of having means for interrupting said therapeutic beam including electronic circuit connecting attenuating means for said therpapeutic beam and said computer with said overlay frame grabber card, said electronic circuit triggering said attenuating means upon sufficient displacement of said retinal location in frame memory of said overlay frame grabber card as determined by digital processing of grabbed said video images; whereby it becomes possible to attenuate said therapeutic laser beam in case of misalignment faster than human reaction time would allow.

4. The combined scanning laser ophthalmoscope-photocoagulator according to claim 1, further comprising the improvement of having means for measuring retinal temperature increase at said retinal location and neighborhood caused by said laser applications,

including second photodetecting means build into said scanning laser ophthalmoscope in similar manner as said photodetecting means, second photodetecting means used for measuring the amount of thermal radiation of near infra-red wavelengths at video rate with the scanning optics of said scanning laser ophthalmoscope; whereby the intensity, location and rate of temperature increase caused by said laser applications at said retinal location is measurable using said computer with said overlay frame grabber card and enabling to attenuate said therapeutic laser beam in case of overdosage faster than human reaction time would allow.

5. The combined scanning laser ophthalmoscope-photocoagulator according to claim 1, further comprising the improvement of having means for simultaneous observation of anterior and posterior segment of the eye, said means for simultaneous observation allowing the continuous visualization on a monitor of said retinal location and its neighborhood and the pivot points of said therapeutic beam, visible beam and invisible beam; whereby it becomes possible to interrupt said therapeutic beam using said computer with said overlay frame grabber card in case of misaligment, permitting further automatic repositioning of said therapeutic beam using the X-Y-Z motorized platform of said scanning laser ophthalmoscope, thereby minimizing the chances of inadvertantly delivering said laser applications outside the anatomical pupil of the eye and facilitating non-contact delivery of said laser applications.

6 A method for measuring retinal function at a precise retinal location using a scanning laser ophthalmoscope, comprising the steps of:

(a) presenting a double colinear laser raster to a retina, whereby a laser raster serves to produce a video representation of said retina on a monitor while a second laser raster is going to be used for projecting a graphical stimulus having a predefined value from a computer controlled overlay graphics card onto said retina;

(b) correcting for any time delay between overlay graphics on said video representation and the projection of said graphical stimlus onto said retina;

(c) determining coordinates of a fiducial landmark on said retina in said video representation prior to presentation of said graphical stimulus;

(d) adjusting in a cartesian manner the video coordinates of said graphical stimulus whereby it becomes possible to project said graphical stimulus at the same said retinal location regardless of eye movements or shifts in fixation;

(e) adjusting the characteristics of said graphical stimulus according to the outcome of previous presentations of said graphical stimulus and following the instructions of a computerized algorithm;

(f) presenting said graphical stimulus;

(g) repeating the above steps from (a) through (g) until a desired endpoint is reached, said endpoint defined as the amount of retinal functioning at said retinal location.

7. A method for measuring retinal function at a precise retinal location using a scanning laser ophthalmoscope according to claim 6, further comprising the improvement of determining said coordinates of a fiducial landmark with the method of normalized gray scale correlation; whereby repeated registration of said fiducial landmark is possible before or after said presentation of graphical stimulus and without the need for manual referencing of said fiducial landmark.

8. A method for measuring retinal function at a precise retinal location using a scanning laser ophthalmoscope according to claim 6, further comprising the steps of:
A. Determining the entry point of the Maxwelian view used by said visible beam;
B. Adjustment of said entry point prior to presentation of said graphical stimulus along the XYZ axes;
C. Repeating steps A through C until a desired endpoint is reached whereby it becomes possible to measure the influence of the orientation of photoreceptors and media opacities in the eye on said retinal function.

9. A method for measuring retinal function at a precise retinal location using a scanning laser ophthalmoscope according to claim 6, wherein the improvement comprises calculation of the intensity of said graphical stimulus using the method of polynomial regression on a curve representing the correlation between a subset of all possible bitlevels for the intensity of said graphical stimulus and the corresponding value of said bitlevels in radiometric or photometric units; whereby it becomes possible to use all said bitlevels for determining said retinal function and efficiently calibrate said scanning laser ophthalmoscope for measuring said retinal function.

10. A method for enlarging the dynamic range of possible intensity values for a graphical stimulus including the steps of:
A. connecting the input of a acousto-optic modulator to a first output channel of a graphics card;
B. connecting the input of a diode laser amplitude modulation circuit to a second output channel of said graphics card;
C. establishing common synchronization between said first output channel and said second output channel;
D. passing the laser beam of said diode laser through said acousto-optic modulator;

E. selecting a first bitlevel for said first output channel and a second bitlevel for said second output channel;

F. modulating said acousto-optic modulator and said diode laser with voltages produced by said graphic card at said first bitlevel and said second bitlevel; whereby it becomes possible to obtain a number of different intensity values for said graphical stimulus equal to the product of said first bitlevel and said second bitlevel.
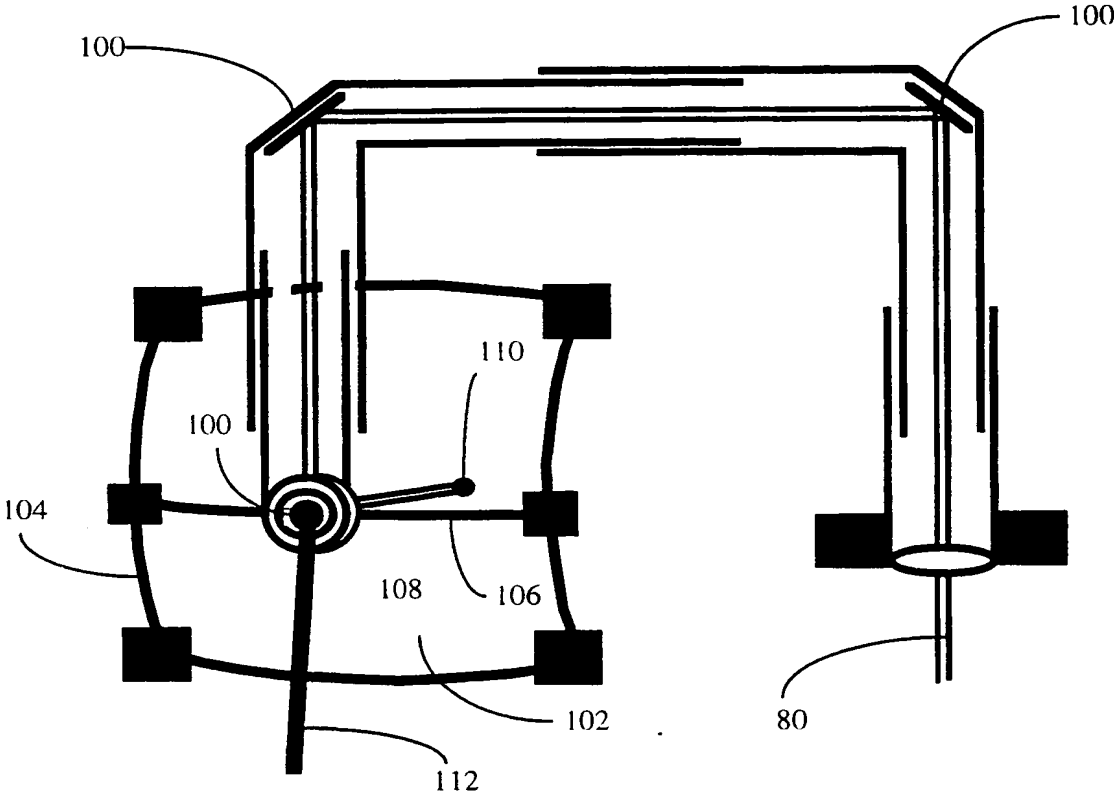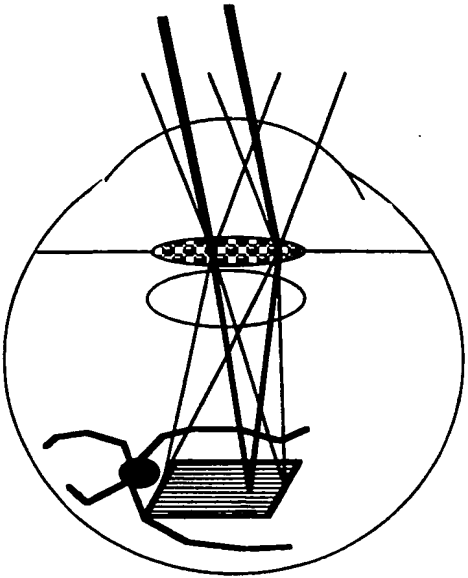
Fig. 1

Fig. 3

Fig. 4

Fig 5

Fig 6

Fig. 7

Fig. 8

$f(x) = 9.778775E\text{-}19 \cdot x^5 + \text{-}1.059504E\text{-}15 \cdot x^4 + 1.427198E\text{-}13 \cdot x^3 +$
$4.322626E\text{-}11 \cdot x^2 + 3.420030E\text{-}9 \cdot x + 7.625050E\text{-}8$
$R0^2 = 9.999931E\text{-}1$

(54) Title: SCANNING LASER OPHTHALMOSCOPE OPTIMIZED FOR RETINAL MICROPHOTOCOAGULATION

(57) Abstract

A combination of scanning laser ophthalmoscope and photocoagulator expands the range of clinical applications of the conventional scanning laser ophthalmoscope, being able of simultaneous imaging and microperimetry with the delivery of therapeutic laser applications to the retina (12) in a preferred non-contact mode. The device, including a therapeutic laser source (80), optic-mechanical Maxwellian view coupling, Maxwellian view control, and real-time electronic registration of the therapeutic beam location, permits precise positioning and dose of the retina applications. Additional safety mechanisms include concurrent temperature measurement of retina application and shutter activation based on digital image processing techniques.

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US97/21453

A. CLASSIFICATION OF SUBJECT MATTER

IPC(6)   : A61B 3/10, 3/00
US CL   :351/205, 221, 246

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 351/205, 221, 246, 200, 206, 208, 210; 359/237, 238

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

Please See Extra Sheet.

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	US 5,568,208 A (VAN DE VELDE) 22 October 1996 (22.10.96), see entire document.	1-10
A	US 5,308,919 A (MINNICH) 03 May 1994 (03.05.94), see entire document.	1-10
A	US 5,152,295 A (KOBAYASHI et al) 06 October 1992 (06.10.92), see entire document.	1-10

☐ Further documents are listed in the continuation of Box C.   ☐ See patent family annex.

*	Special categories of cited documents:	"T"	later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"A"	document defining the general state of the art which is not considered to be of particular relevance		
"E"	earlier document published on or after the international filing date	"X"	document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"L"	document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)	"Y"	document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"O"	document referring to an oral disclosure, use, exhibition or other means		
"P"	document published prior to the international filing date but later than the priority date claimed	"&"	document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
10 MAY 1998	1 9 JUN 1998

Name and mailing address of the ISA/US	Authorized officer
Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231	HUY MAI
Facsimile No. N/A	Telephone No. (703) 308-4874

Form PCT/ISA/210 (second sheet)(July 1992)*

B. FIELDS SEARCHED
Electronic data bases consulted (Name of data base and where practicable terms used):

APS
search terms: scanning laser ophthalmoscope, photocoagulator, retina, detect?, therapeutic laser source, micromanipulator, coupling, filter, synchronizing, modulating